negative pressures within the interior chamber, whereby the alternating positive and negative pressures are conducted by the orifices to the top surface of the vacuum fixture at locations corresponding to the bottoms of the wells to create a micromixing effect in the wells.

Please add the following new claims 31- 32:

31. (New) The assembly of claim 22, wherein each well containing an array formation area at its bottom.

32. (New) The assembly of claim 22, wherein the microplate further comprises a rigid frame detachably attached to the flexible material, wherein the rigid frame is adapted for mounting the microplate on the top surface of the vacuum fixture.

REMARKS:

Claims 1-22 and 25 are amended; marked up versions of the amended claims are attached hereto pursuant to 37 C.F.R. § 1.121(c)(ii). New claims 31-32 are added. No new matter is introduced. Claims 1-25 and 31-32 are pending in the application. Reexamination and reconsideration of the application, as amended, are respectfully requested.

The Examiner objected to the specification due to informalities. In response, applicant has carefully reviewed the specification and has made the appropriate corrections. No new matter has been introduced.

Claims 1-25 are rejected under 35 U.S.C. § 112, second paragraph, as being indefinite and vague. In particular, claim 1 was rejected for the use of the term "activated." This rejection is respectfully traversed.

The Examiner deemed unclear "how the areas are 'activated' for the immobilization of biorecognition material." In response, applicant respectfully draws the Examiner's attention to page 6, line 29-page 7, line 5, of the specification and to dependent claim 14. The specification and claim 14 stipulate that the array

formation areas may be activated for the immobilization of biorecognition materials by direct surface treatment, placement of activated inserts, or adsorption of an activated coating to the surface of the array formation areas. The specification further explains on page 6, lines 17- 22, that the biorecognition materials may be attached to the array formation areas by covalent, non-covalent or any other suitable means, such as affinity interaction with biorecognition molecules attached to the site. Additionally, on page 13, lines 4-11, the specification provides an example of such activation (surface activation with acyl fluoride groups). Accordingly, applicant submits that the specification clearly defines the term "activated" as "made available for the immobilization of biorecognition materials."

The Examiner also rejected claim 8 for using the term "one or more array formation areas" and claims 9 and 19 for reciting the term "an array formation area." The Examiner appeared to believe that it is unclear in claims 8, 9, and 19 whether the recited array formation areas are the same as in claim 1. In response, applicant amended claims 8, 9 and 19 to clarify that they recite the same array formation areas as those recited in claim 1.

The Examiner rejected claim 14 as lacking antecedent basis for the term "the surface area of." The Examiner also rejected claim 18 for reciting measurement standards in parenthesis. In response, applicant amended claims 14 and 18 to address these rejections.

Claims 1-5 and 9-13 are rejected under 35 U.S.C. § 102(b) as being anticipated by Donald B. Rising, U.S. Patent No. 5,554,536 (the '536 patent). This rejection is respectfully traversed.

Independent claim 1, as amended, is directed to an assembly for a microarray assay device. The device comprises a microplate having a plurality of discrete <u>array formation areas</u>, each formed of a <u>flexible material</u> and a <u>vacuum fixture</u> defining a top surface, and an interior chamber connectable to a vacuum source. The <u>microplate is mounted on the top surface of the vacuum fixture</u> so that the array formation areas are supported on the top surface of the vacuum fixture. The vacuum fixture further defines a <u>plurality of orifices connected to the interior</u>

chamber and opening at the top surface at locations corresponding to the array formation areas when the microplate is mounted on the top surface of the vacuum fixture.

As explained on page 8, line 30-page 9, line 7, of the instant specification, when a vacuum is drawn in the interior chamber of the vacuum fixture, the vacuum is communicated via the orifices to create a negative pressure to hold the bottom of the array formation areas, such as wells, firmly against the top surface of the fixture. As a result, even though the microplate is formed of a flexible material, the bottom portions of the wells maintain a high precision flatness to facilitate high-resolution printing and reading of the microarrays. A high degree of flatness of less than 0.0001-inch variation across the array formation areas may be obtained. In addition, as discussed on page 9, lines 16-22, of the instant specification, by connecting the vacuum fixture of the present invention to a peristaltic pump which generates alternating positive and negative pressures, the present invention allows the solution held in the wells to be mixed uniformly.

The Description of the Related Art section of the instant invention (pages 1-2) explains that conventional arrays are either printed on glass slides, which results in low throughput and poor data quality and reproducibility, or in the microwells of molded polymer titer plates, which, due to thermal warp, fail to provide sufficient flatness. Due to the lack of flatness, conventional molded titer plates do not allow accurate dispensing of nanoliter amounts of fluids using pin printers. Further, when the plates are heated, a warp also creates variable air gaps between the wells and the heating fixture on which the plate is placed. These air gaps lead to variable thermal resistance from well to well, which leads to difficulties in controlling incubation or hybridization and difficulties in controlling incubation or hybridization temperature from one array to another. The assembly of the present invention unexpectedly overcomes the disadvantages of the prior art. The instant assembly provides a high-throughput array processing, allows for flat printing surfaces and results in low well-to-well temperature variations during thermal incubation.

The '536 patent does not anticipate instant claim 1 because it does not teach a vacuum fixture. The '536 patent is not relied upon by the Examiner for teaching a vacuum fixture. The Examiner cites the '536 patent for the teaching of a microwell membrane plate with a tray for conducting biological analysis.

The '536 patent does not make instant claim 1 obvious. The '536 patent has no teaching whatsoever of printing biomolecular arrays in the wells of plastic plates and warp problems associated with such printing, much less of a vacuum fixture used in association with a flexible microplate to prevent warp and achieve the desired flatness of the bottoms of the wells. Therefore, claim 1 and its dependent claims 2-5 and 9-13 are patentable over the '536 patent.

Claims 1-5 and 9-15 are rejected under 35 U.S.C. § 102(e) as being anticipated by Coassin et al., U.S. Patent No. 6,232,114 (the '114 patent). This rejection is respectfully traversed.

Similarly to the '536 patent, the '114 patent does not anticipate instant claim 1 because it does not teach a vacuum fixture. The '114 patent is not relied upon by the Examiner for teaching a vacuum fixture. The Examiner cites the '114 patent for the teaching of polymeric multi-well plates that are used for fluorescence measurement of biological samples.

The '114 patent does not make instant claim 1 obvious. The '114 patent has no teaching whatsoever of printing biomolecular arrays in the wells of plastic plates and warp problems associated with such printing, much less of a vacuum fixture used in association with a flexible microplate to prevent warp and achieve the desired flatness of the bottoms of the wells. Therefore, claim 1 and its dependent claims 2-5 and 9-15 are patentable over the '114 patent.

Claim 6 is rejected under 35 U.S.C. § 103(a) as being unpatentable over the '536 patent or the '114 patent in view of Ashok R. Sandai, U.S. Patent No. 5,516,490 (the '490 patent). This rejection is respectfully traversed.

As discussed above, claim 1 is patentable over the '536 patent and the '114 patent. The '490 patent cannot remedy the defects of the '536 patent and the '114 patent, and is not relied upon by the Examiner for such. The Examiner cites the

'490 patent for the teaching of a gasket being disposed over the substrate and sealed thereto.

The '490 patent, either alone or in combination with the '536 patent or the '114 patent, does not make instant claim 1 obvious. The '490 patent has no teaching whatsoever of printing biomolecular arrays in the wells of plastic plates and warp problems associated with such printing, much less of a vacuum fixture used in association with a flexible microplate to prevent warp and achieve the desired flatness of the bottoms of the wells. Therefore, claim 1 is patentable over a combination of the '536, the '114, and the '490 patents. Claim 6 depends from claim 1 and is patentable over a combination of the '536 patent with the '114 patent, or the '490 patents for at least the same reasons as claim 1.

Claims 7 and 8 are rejected under 35 U.S.C. § 103(a) as being unpatentable over the '536 patent or the '114 patent in view of Patrick Gaillard, U.S. Patent No. 5,948,363 (the '363 patent). This rejection is respectfully traversed.

As discussed above, claim 1 is patentable over the '536 patent and the '114 patent. The '363 patent cannot remedy the defects of the '536 patent and the '114 patent, and is not relied upon by the Examiner for such. The Examiner cites the '363 patent for the teaching of a rigid frame that is detachable from the well strips.

The '363 patent, either alone or in combination with the '536 patent or the '114 patent, does not make instant claim 1 obvious. The '363 patent has no teaching whatsoever of printing biomolecular arrays in the wells of plastic plates and warp problems associated with such printing, much less of a vacuum fixture used in association with a flexible microplate to prevent warp and achieve the desired flatness of the bottoms of the wells. Therefore, claim 1 is patentable over a combination of the '536, the '114, and the '363 patents. Claims 7 and 8 depend from claim 1 and are patentable over a combination of the '536, the '114, and the '363 patents for at least the same reasons as claim 1.

Claims 16-18 are rejected under 35 U.S.C. § 103(a) as being unpatentable over the '536 patent or the '114 patent in view of Mathus et al., U.S. Patent No. 5,858,309 (the '309 patent). This rejection is respectfully traversed.

As discussed above, claim 1 is patentable over the '536 patent and the '114 patent. The '309 patent cannot remedy the defect of the '536 patent and the '114 patent, and is not relied upon by the Examiner for such. The Examiner cites the '309 patent for the teaching of microplates and methods for manufacturing microplates to allow UV radiation to pass through the bottom of the wells. Specifically, the Examiner cites the '309 patent for teaching a microplate with a material thickness of 7.5 mils.

The '309 patent, either alone or in combination with the '536 patent or the '114 patent, does not make instant claim 1 obvious. The '309 patent has no teaching whatsoever of printing biomolecular arrays in the wells of plastic plates and warp problems associated with such printing, much less of a vacuum fixture used in association with a flexible microplate to prevent warp and achieve the desired flatness of the bottoms of the wells. Therefore, claim 1 is patentable over a combination of the '536 patent with the '114 patent or the '309 patent. Claims 16-18 depend from claim 1 and are patentable over a combination of the '536, the '114, and the '309 patents for at least the same reasons as claim 1.

Claims 19-24 are rejected under 35 U.S.C. § 103(a) as being unpatentable over the '536 patent or the '114 patent in view of Mohan et al., U.S. Patent No. 5,888,830 (the '830 patent). This rejection is respectfully traversed.

As discussed above, claim 1 is patentable over the '536 patent and the '114 patent because claim 1 requires a vacuum fixture. Since independent claim 22 also requires a vacuum fixture, it is patentable over the '536 and the '114 patents.

The '830 patent cannot remedy the defects of the '536 and the '114 patents. Claims 1 and 22 require a vacuum fixture defining a top surface and an interior chamber connectable to a vacuum source, wherein the microplate is mounted on the top surface of the vacuum fixture so that the array formation areas (or wells in claim 22) conform to the top surface of the vacuum fixture. The vacuum fixture further includes a plurality of orifices connected to the interior chamber and opening at the top surface at locations corresponding to the array formation areas (or wells) when the microplate is mounted on the top surface of the vacuum fixture.

As explained above, such structure unexpectedly allows achieving the desired flatness of the array formation areas (or bottom of each well) when a vacuum is drawn in the interior chamber.

The '830 patent does not teach or suggest the assembly of claims 1 and 22. First, the '830 patent does not teach microplates as generally defined in the art and described in the instant specification. Those skilled in the art usually associate the term "microplate" with structures having arrays of wells as those, for example, described in the '536 patent that was cited by the Examiner. The wells have closed bottoms to retain reaction solutions as in the '536 patent and to allow printing of the arrays as in the present invention.

The '830 patent does not teach any structures containing closed bottom wells. To the contrary, the '830 patent teaches an apparatus in which reaction vessels 12 have open syringe tips 13 to allow for drainage of the fluids contained therein. The apparatus also comprises a manifold valve block 30 with passages 50 for receiving the syringe tips 13 of reaction vessels 12 and allowing fluid contained in the reaction vessels to pass through the valve block (column 11, lines 21-35). The valve block is attached to a channel block 34 that allows the collection of fluids from the vessels into a drainage system 35 by utilizing a vacuum pump connected to the drainage system (column 10, lines 37-57). Thus, neither a plurality of reaction vessels nor the valve block of the '830 patent form a microplate as understood by those skilled in the art.

Second, even if the valve block with passages 50 were considered to be similar to a microplate with wells and if the channel block were considered to be similar to a vacuum fixture, one would not have obtained the assembly of the present invention that requires the array formation areas (or well bottoms) to conform to the top surface of the vacuum fixture. In the '830 patent, the passages 50 receive valve inserts 51 with lateral bores 54 and with a female Luer connector 52 at the top and a male Luer connector 53 at the bottom. Each female Luer connector 52 serves as an inlet into the manifold valve block 30 and receives the syringe tip 13 of one reaction vessel 12. Each male Luer connector 53 serves as an

outlet for fluid passage from the manifold valve block 30 (column 11, lines 21-47). Thus, neither passages 50 nor inserts 51 provide continuous surface areas similar to well bottoms that may conform to another surface, such as that of the vacuum fixture.

Furthermore, the '830 patent does not provide a vacuum fixture having a top surface conforming to the well bottoms or array formation areas. Instead, it teaches a drainage channel block 34 with channels 65 <u>aligned</u> with rows of the male Luer connectors 53 of the valve inserts 51 in the manifold valve block 30 so that when the valve inserts are opened, the liquid therein simultaneously drains into the array of interconnected channels (column 11, lines 58-67). Thus, instead of a vacuum fixture having a top surface <u>conforming</u> to the well bottoms or array formation areas, the '830 patent teaches drainage channels simply <u>aligned</u> with the passages 50 of the valve block.

Similarly, a cleavage block 120, which substitutes the channel block 34 after the washing step, does not have a top surface conforming to the passages 50. The cleavage block includes a vial tray rack 122 mounted in a cavity 123 of the cleavage block 120. The vial rack 122 is loaded with vials 128 for receiving the reaction products from the reaction vessels 12 upon simultaneously opening the valves 51 in the manifold valve block 30 (column 13, lines 55-65). Thus, instead of a vacuum fixture having a top surface <u>conforming</u> to the well bottoms or array formation areas, the '830 patent teaches vials 128 simply <u>aligned</u> with the passages 50 of the valve block.

<u>Third</u>, neither the channel block 34 nor the cleavage block 120 has a plurality of orifices connected to the interior chamber and opening at the top surface at locations corresponding to the array formation areas. The channel block 34 does not have an internal chamber and does not have orifices corresponding to each passageway. Instead, channels of the channel block are simply aligned with the passages 50 of the valve block to allow the drainage of liquid when the valves are open and the vacuum is applied to the channels (column 11, lines 58-67).

Similarly, the cleavage block does not have orifices corresponding to each passageway. Instead, with the opening of the insert valves 51, a vacuum is applied to a single quick connect fitting 60 by the vacuum pump 39 which causes the solvent in the reaction vessels 12 to flow into the array of ninety-six vials 128 (column 15, lines 2-10). Therefore, the '830 patent does not anticipate or suggest the vacuum fixture, the microplate, or the assembly of claims 1 and 22.

Additionally, the device of the '830 patent cannot be adapted for the use with conventional microplates or microplates of other patents cited by the Examiner. As discussed above, while conventional microplates have closed wells, the '830 patent requires structures with open bottoms for the drainage of fluids. Thus, it is impossible to apply the teachings of the '830 patent to the conventional microplates without destroying their structure.

Also, neither the '830, the '536, nor the '114 patent discusses a need for providing flat well bottom surfaces for bioarray printing. Thus, based on the teachings of the cited patents, those skilled in the art would not have combined the teachings of the '830, the '536, and the '114 patents to arrive at instant claims 1 and 22. Therefore, claims 1 and 22 are patentable over a combination of the '830, the '536, and the '114 patents. Claims 19-21 and 23-24 depend from claims 1 and 22 and, thus, are patentable over the '830, the '536, and the '114 patents for at least the same reasons as claims 1 and 22.

Claim 25 is rejected under 35 U.S.C. § 103(a) as being unpatentable over the '536 patent or the '114 patent in view of the '830 patent and in further view of Stylli et al., U.S. Patent No. 5,985,214 (the '214 patent). This rejection is traversed.

As discussed above, claim 22 is patentable over the '536, the '114, and the '830 patents. The '214 patent cannot remedy the defects of the '536, the '114, and the '830 patents, and is not relied upon by the Examiner for such. The Examiner cites the '214 patent for the teaching of a peristaltic pump.

The '214 patent, either alone or in combination with the '536, the '114, and the '830 patents, does not make the instant claim 1 obvious. The '214 patent has no teaching whatsoever of printing biomolecular arrays in the wells of plastic plates

and warp problems associated with such printing, much less of a vacuum fixture used in association with a flexible microplate to prevent warp and achieve the desired flatness of the bottoms of the wells. Therefore, claim 22 and its dependent claim 25 is patentable over a combination of the '536, the '114, the '830, and the '214 patents.

In view of the foregoing, it is respectfully submitted that the application is in condition for allowance. Reexamination and reconsideration of the application, as amended, are requested.

If for any reason the Examiner finds the application other than in condition for allowance, the Examiner is requested to call the undersigned attorney at the Los Angeles, California telephone number (213) 337-6700 to discuss the steps necessary for placing the application in condition for allowance.

If there are any fees due in connection with the filing of this response, please charge the fees to our Deposit Account No. 50-1314.

Respectfully submitted,
HOGAN & HARTSON L.L.P.

Date: October 31, 2002

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Version with markings to show changes made:

IN THE SPECIFICATION:

Please replace the second paragraph on page 7, lines 12-20, with the following text:

Figs. 1(a) - 1(c) illustrate an A^2 plate in the form of a shallow multi-well microplate according to one embodiment of the present invention. As shown in Fig. 1(a) (top view) and Fig. 1(b) (cross-sectional view along the line A-A'), the A^2 plate 10 is formed of a tray 12, such as a molded tray, held at its edges by a rigid frame 14, such as a clam shell frame. The tray 12 is formed with an array of depressions or wells 16, which may be surface-treated for binding of biorecognition materials. Fig. 1(c) shows details of the clam shell frame that holds the tray at the edges. The tray may be clamped at all edges or some of the edges. Preferably, the tray is detachably mounted on the frame. This frame is preferably adapted for use with robotic tools such as the [Biomek] BIOMEK® Gripper Tool [▤].

Please replace the last paragraph on page 8, lines 26-31, with the following text:

The fixture 32 has an interior chamber 34 connectable to a vacuum source (not shown) via channels 34a, and a plurality of orifices 36 located on the top surface and connected to the interior [number] chamber 34. The orifices 36 are located within the depressions 38 in the embodiment of Fig. 3(a), or at locations corresponding to the bottom of the wells 16 in the embodiment of Fig. 3(c). When a vacuum is drawn in the interior chamber 34, the vacuum is communicated via the orifices 36 to create a negative pressure to hold the

Please replace the second full paragraph on page 12, lines 6-30, with the following text:

The application of the A^2 plate and the fixture apparatus in the microarray assay system and process is described with reference to Fig. 9. The microarray

assay system 90 includes the following modular units: a microarray printer 92, a robotics workstation 94 such as Biomek robotic station, a hybridization hotel 96, and transport system 98 such as an [Orca™] ORCA® arm and slide rail. The various modular units have been used in microarray assay systems that use conventional glass slide microarrays or conventional multi well assays, and may be adapted to work with the A^2 plate and fixture apparatuses. The printer 92 is used to print microarrays of probes such as cDNA, oligo, protein, etc. onto the array of arrays microplate 91. When printing, the A^2 plate is positioned on the vacuum fixture and the vacuum is drawn. An array spotter, such as Cartesian's BioDot Arrayer, deposits an array of probes inside each well. Arrays of many hundreds of probes can be printed. After printing, the microplate is transported either to the robotic workstation 94 for processing of samples under automated hybridization or incubation, or transferred to the hybridization hotel 96 for storage. For hybridization and incubation, samples and reagents are deposited into the microplate on the robotic workstation 92. A fixture having temperature control and/or micromixing capabilities may be used for this process. After the microplate is prepared for hybridization or incubation, it is transferred using the transport system 98 to the hybridization hotel 96, where hybridization of the probes and targets (for cDNA arrays), or incubation (for protein arrays) is allowed to proceed. The hybridization hotel 96 is a high-capacity incubator that provides a programmable humidity and temperature control. Upon completion of hybridization or incubation, the plate is removed from the hotel 96 and returned to the workstation 94 for further processing such as imaging. During this process, the plate is rinsed and signal development reagents dispensed into the wells; subsequently, the plate is again rinsed and either returned to the hotel for storage or transferred to a reading station.

IN THE CLAIMS:

Please replace the text of claims 1-22 and 25 with the following text:

1. (Amended) [A microplate] An assembly for a microarray assay device, comprising:

a microplate having a plurality of discrete array formation areas each formed of a flexible material and activated for immobilization of biorecognition materials, and barriers formed between the array formation areas to restrict fluid cross-flow therebetween; and

a vacuum fixture defining a top surface and an interior chamber connectable to a vacuum source, wherein the microplate is mounted on the top surface of the vacuum fixture so that the array formation areas conform to the top surface of the vacuum fixture, the vacuum fixture further defining a plurality of orifices connected to the interior chamber and opening at the top surface at locations corresponding to the array formation areas when the microplate is mounted on the top surface of the vacuum fixture.

2. (Amended) The [microplate] assembly of claim 1, wherein the barriers are walls formed of the flexible material, hydrophobic patches, troughs, gaskets, or pedestals formed between the array formation areas.

3. (Amended) The [microplate] assembly of claim 1, wherein the barriers have a height of less than about 4 mm.

4. (Amended) The [microplate] assembly of claim 1, [comprising] wherein the microplate comprises a tray formed of the flexible material, the tray having a plurality of discrete wells formed therein, each well containing an array formation area at its bottom, wherein the bottom of each well is supported on the top surface of the vacuum fixture.

5. (Amended) The [microplate] assembly of claim 1, [comprising] wherein the microplate comprises a tray formed of the flexible material, the tray having a peripheral depression surrounding one or more array formation areas.

6. (Amended) The [microplate] assembly of claim 1, [comprising] wherein the microplate comprises a support plate, a flat substrate formed of the flexible material disposed over the support plate, and a gasket defining a plurality of holes, the gasket being disposed over the substrate and sealed thereto, where each area of the substrate exposed by a hole of the gasket contains an array formation area.

7. (Amended) The [microplate] assembly of claim 1, [further comprising] wherein the microplate further comprises a rigid frame detachably attached to the flexible material, wherein the rigid frame is adapted for mounting the microplate on the top surface of the vacuum fixture.

8. (Amended) The [microplate] assembly of claim 7, [further comprising] wherein the microplate further comprises a plurality of rigid hangers, and a plurality of well strips formed of the flexible material, each well strip being pressed-fitted into a rigid hanger, each well strip containing one or more array formation areas.

9. (Amended) The [microplate] assembly of claim 1, further comprising a plurality of microarrays of biorecognition materials, each microarray being formed within an array formation area.

10. (Amended) The [microplate] assembly of claim 9, wherein the biorecognition materials include biomolecules, cells or cellular components.

11. (Amended) The [microplate] assembly of claim 9, wherein the biorecognition materials are labeled.

12. (Amended) The [microplate] assembly of claim 9, wherein each array contains from 1 to 1536 elements of biorecognition materials.

13. (Amended) The [microplate] assembly of claim 1, wherein the array formation areas are activated for immobilization of biorecognition materials by covalent interaction, noncovalent interaction or affinity interaction.

14. (Amended) The [microplate] assembly of claim 1, where the array formation areas are activated by direct surface treatment, placement of activated inserts, or adsorption of an activated coating to the surface of the areas.

15. (Amended) The [microplate] assembly of claim 1, wherein the flexible material is a thermal formable polymer material and the microplate is formed by vacuum forming or injection molding.

16. (Amended) The [microplate] assembly of claim 1, wherein the flexible material has a thickness of about 0.1 to 100 mils.

17. (Amended) The [microplate] assembly of claim 16, wherein the flexible material has a thickness of about 1 to 10 mils.

18. (Amended) The [microplate] assembly of claim 1, wherein the flexible material has a flexural modulus [(ASTM D790)] of about 170-220 Ksi, a Shore D hardness [(ASTM D 2240)] of about 65-80, and a deflection temperature at 66 Psi of about 100-200°F.

19. (Amended) The [microplate] assembly of claim 1, further comprising a lid formed of a plurality of caps each corresponding to an array formation area.

20. (Amended) The [microplate] assembly of claim 19, wherein each cap comprises a gas inlet port, a gas outlet port, and a gas diffusion member disposed on an inside of the cap.

21. (Amended) The [microplate] <u>assembly</u> of claim 20, wherein each cap further comprises a temperature control element.

22. (Amended) An assembly for a microarray assay device, comprising:

a microplate [of claim 1] <u>having a plurality of wells formed of a flexible material and having continuous flat bottoms;</u>

[a rigid frame attached to a periphery of the microplate;] and

a vacuum fixture defining a top surface and an interior chamber connectable to a vacuum source, wherein the [rigid frame is adapted for mounting the] microplate <u>is mounted</u> on <u>the</u> top <u>surface</u> of the vacuum fixture so that the [array formation areas are] <u>bottom of each well</u> [supported on] <u>conforms to</u> the top surface of the vacuum fixture, the vacuum fixture further defining a plurality of orifices connected to the interior chamber and opening at the top surface at locations corresponding to the [array formation areas] <u>bottoms of the wells</u> when the microplate is mounted on the top surface of the vacuum fixture [via the rigid frame].

25. (Amended) The assembly of claim 22, further comprising a peristaltic pump connected to the interior chamber for generating an alternating positive and negative pressures within the interior chamber, whereby the alternating positive and negative pressures are conducted by the orifices to the top surface of the vacuum fixture at locations corresponding to the [array formation areas] <u>bottoms of the wells</u> to create a micromixing effect <u>in the wells</u>.